

Amendments to the Claims/Listing of Claims

Please amend claims 14 and 19, and cancel claims 4, 5, 9, 16, 17, 23-30 and 34-37 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Original) A composition comprising the ligand binding domain of a farnesoid X receptor (FXR) in crystalline form.
2. (Original) A composition according to claim 1 further comprising a ligand of said FXR.
3. (Original) A composition according to claim 2, wherein said ligand is selected from the group consisting of fexaramine, fexarine, fexarene and GW4064.
- 4.-5. Cancelled.
6. (Original) A composition according to claim 1 as described by the structure coordinates set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.
7. (Original) A composition according to claim 2 as described by the structure coordinates set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and said ligand.
8. (Original) A composition according to claim 2, wherein the crystals belong to space group $P2_12_12_1$ with unit cell dimensions of about:
 $a = 37 \text{ \AA}$, $b = 57 \text{ \AA}$, $c = 117 \text{ \AA}$,
 $\alpha = 90^\circ$, $\beta = 90^\circ$, and $\gamma = 90^\circ$.
9. Cancelled.

10. (Original) A composition according to claim 1, wherein said ligand binding domain comprises amino acid residues 248 – 476 of SEQ ID NO:1.

11. (Original) A computer for producing a three-dimensional representation of a farnesoid X receptor (FXR) molecule or molecular complex or a homologue of said FXR molecule or molecular complex, wherein said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex comprises a ligand binding domain defined by structure coordinates obtained from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex, said computer comprising:

(i) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex;

(ii) a working memory for storing instructions for processing said computer-readable data;

(iii) a central-processing unit coupled to said working memory and to said computer-readable data storage medium for processing said computer-machine readable data into said three-dimensional representation; and

(iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.

12. (Original) A computer according to claim 11, wherein said structure coordinates are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.

13. (Original) A computer for determining at least a portion of the structure coordinates corresponding to X-ray diffraction data obtained from a farnesoid X receptor (FXR) molecule or molecular complex or a homologue of said FXR molecule or molecular complex, said computer comprising:

(i) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises at least a portion of the structure coordinates of Appendix 1;

(ii) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises X-ray diffraction data obtained from said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex;

(iii) a working memory for storing instructions for processing said computer-readable data of (i) and (ii);

(iv) a central-processing unit coupled to said working memory and to said computer-readable data storage medium of (i) and (ii) for performing a Fourier transform of the machine readable data of (i) and for processing said computer-readable data of (ii) into structure coordinates; and

(v) a display coupled to said central-processing unit for displaying said structure coordinates of said FXR molecule or molecular complex.

14. (Currently amended) A method of predicting a molecule capable of binding to a farnesoid X receptor (FXR) molecule, said method comprising:

modeling a test molecule that potentially interacts with the ~~ligand binding domain of said FXR molecule~~ composition of claim 1, wherein said ligand binding domain is defined by a plurality of structure coordinates of the ligand binding domain of a FXR molecule or a fragment thereof,

wherein said structure coordinates are derived from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex.

15. (Original) A method according to claim 14, wherein said plurality of structure coordinates are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.

16.-17. Cancelled.

18. (Original) A method according to claim 14, wherein said test molecule is developed using a computer algorithm to predict a three-dimensional representation of said test molecule interacting with a FXR based upon a three-dimensional representation of a FXR molecule or fragment thereof.

19. (Currently amended) A method of identifying a compound with agonist, partial agonist, or antagonist activity ~~for~~ with respect to a farnesoid X receptor (FXR) molecule, said method comprising:

(a) modeling a test compound that potentially interacts with the ligand binding domain of said FXR molecule or a fragment thereof, wherein said ligand binding domain is defined by a plurality of structure coordinates of the ligand binding domain of a FXR molecule or a fragment thereof,

wherein said plurality of structure coordinates are derived from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex; and

(b) determining the ability of said test compound to ~~activate~~ modulate the activity of said FXR molecule in the optional presence of a known FXR agonist.

20. (Original) A method according to claim 19, wherein said plurality of structure coordinates are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.

21. (Original) A compound identified by the method of claim 19.

22. (Original) A pharmaceutical composition comprising a compound identified by the method of claim 19 and a pharmaceutically acceptable carrier therefor.

23.-30. Cancelled.

31. (Original) A method for determining whether a test compound is capable of binding to the ligand binding domain of a farnesoid X receptor (FXR) molecule, said method comprising:

- (a) determining the points of interaction between the ligand binding domain of a FXR, and one or more known ligand(s) therefor; and
- (b) analyzing said test compound to determine whether similar points of interaction exist between said test compound and said ligand binding domain.

32. (Original) A method according to claim 31, wherein step (a) utilizes a plurality of structure coordinates derived from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex to define said points of interaction.

33. (Original) A method according to claim 32, wherein said structure coordinates are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and said ligand(s).

34.-37. Cancelled.